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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,150	07/02/2007	Paul Kemp	50393/007001	5682

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EXAMINER	
BERTOGLIO, VALARIE E	
ART UNIT	PAPER NUMBER
1632	

NOTIFICATION DATE	DELIVERY MODE
12/21/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/589,150	KEMP ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *25 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21 and 55-128* is/are pending in the application.

4a) Of the above claim(s) *111-128* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21 and 55-110* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 August 2009* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/07/2006;06/11/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of Group I, claims –21 and 55-110 in the reply filed on 11/25/2009 is acknowledged. The traversal is on the ground(s) that Groups I-III relate to a product, process of manufacture and process of using the product. This is not found persuasive because the special technical feature of the groups is not a contribution over the art.

The requirement is still deemed proper and is therefore made FINAL.

Claims 111-128 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 11/25/2009.

Claim Rejections - 35 USC § 112-1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-21 and 55-110 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but

rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The claims are drawn to a wound healing composition comprising cells having specific recited gene expression phenotypes. Some claims limit some of the conditions for making the composition. However, most limitations are drawn to characteristics of the composition itself.

The specification teaches making a composition comprising fibroblasts, fibrinogen, aprotinin, thrombin and calcium chloride (Example 1). The specification teaches incubation of the composition over 16-24h prior to packaging page 32). Packaging is discussed in Example 3, pages 34-36. At Example 4, the specification teaches gene expression analysis by differential display of fibroblasts in a collagen matrix, a fibrin matrix, and no matrix as well as the 'wound healing composition' (the fibrinogen, aprotinin, thrombin and calcium chloride composition of Example 1). Gene expression analysis was performed after various storage periods and the storage periods appear to have differentially affected gene expression. Thus, the composition is stored for up to 14 days would differ from those incubated more than 14 days. The results, reported in Table 4, combine compositions that are made with collagen, fibrin or no matrix protein and compare gene expression profiles relative to a housekeeping gene, RPL32. Such a comparison correlates to claims 1-21 and 55-84. Claims 85-110 relate to comparison to different controls, i.e. different protein matrices (collagen, no matrix protein). Data is presented in Table 6 (Example 5), however, the units are not presented and the control for comparison is not presented. Thus, it cannot be determined what the numbers in Table 6 represent or how they correlate to claims 85-110. Furthermore,

the claims break down the storage times to smaller increments. It is presumed that gene expression levels will differ at these various claimed times. However, data in the specification is pooled for less than, and greater than, 14 days. The claims recite these gene expression values in various claims. However, as the samples are pooled samples, one of skill in the art would not know what exact conditions resulted in the claimed ranges. It is not clear how many of the cells were grown on collagen, how many on fibrin, etc.

Furthermore, the specification has failed to demonstrate a "wound healing" phenotype, resulting from the claimed cells, that differs from fibroblasts in general. It cannot be determined, given the guidance in the specification, which conditions result in a wound healing phenotype. It appears the claims are drawn to a composition of cells that is changing in gene expression over time. It is not clearly enabled by the specification which cells and which gene expression levels will result in a desired wound healing phenotype.

Additionally, claims 5,16,61,62,66,92-93 (for example), are not fully supported by the specification as written. The claim requires incubation within a protein-rich environment for up to 14 days to allow development of a wound healing phenotype. This encompasses incubation at 37 degrees, for which the specification only teaches incubation for 16-24 hours before packaging and incubating at a lower temperature, i.e. 4 degrees. The specification fails to clearly establish when the 'wound healing' phenotype develops.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-16 and 61-62 67-69,92-95 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 is unclear as it is a product claim that contains method claim language. It is not clear if the composition has been stored under the recited condition, or whether it was already stored at those conditions. It's not clear what requirements need be met to fulfill the limitations of the claims.

Claim 5 is unclear. It is not clear if the cells "are" incubated in a protein-rich environment in the claimed composition or if the cells "were" incubated under the claimed parameters in making the composition.

Likewise, it is unclear if, in claims 67-69, the composition "is" incubated for the recited period or if it "was" incubated as claimed prior to formation of the claimed product.

Claim 16,61-62 and 92-95 are unclear. It is not clear if the claim encompasses cells during the claimed storage period or if it is intended to encompass a composition after the storage period has expired.

Claim 14 is unclear as it is not clear how the incubation can occur if the cells are not cast into the support matrix before incubation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-15,17-21, 55-60,63-65,67-73,76-78,81-91,95-99,102-104,107-110 are rejected under 35 U.S.C. 102(b) as being anticipated by Meana et al, (1998; IDS).

The instant rejection is not in contradiction to the above lack of enablement rejection. The claims are drawn to a composition and the art is applied to the extent that it appears to read on the claimed composition, particularly claims lacking any required methodology in obtaining the specifically recited gene expression profile. The specification fails to clearly set forth which methodology results in which

expression levels, hence the lack of enablement. However, the art, as set forth below, appears to teach the same methodology, which would inherently result in the claimed characteristics.

Claims 1-4 are drawn to a wound healing composition with various recited gene expression characteristics. Claims 5-15 recite limitations regarding the protein-rich matrix upon which the cells are deposited. Claim 17 requires the cells be mammalian. Claim 63 requires the cells be human. Claims 18 and 64 require the cells be substantially fibroblasts or dermal fibroblasts (claim 19; human dermal fibroblasts, claim 65), substantially excluding keratinocytes (claim 20). Claim 21 defines the composition as one in which the cells are human dermal fibroblasts within a matrix formed by thrombin-mediated polymerization of fibrinogen, incubated for 16-24 hours at 37 degrees. Claims 55-57 limit the expression levels of various genes. Claims 58-60 limit the matrix composition. Claims 70-71 recited characteristics of the cells. Claims 71-73 and 76-77 limit characteristics of the matrix. Claim 78 recites limitations regarding packaging. Claims 81-84 and 107-110 recite uses for the claimed composition; *recitation of intended use has no patentable weight.* Claims 85-91 appear to be drawn to the same composition but recite gene expression characteristics in comparison to various controls. Claims 95-97 recite incubation periods. Claims 98-103 recite characterstics of the matrix. Claim 104-106 limit the packaging.

Meana teaches, in section 2.2 at page 622, teaches isolating human foreskin fibroblasts and culturing them on fibrin-containing gel between the 4th and 12th passage. The fibrin gel was made using 3ml of fibrinogen and 500,000 human fibroblasts and aprotinin in addition to thrombin and calcium chloride, the same conditions discussed in the specification (see page 28, Table 1). The gel was covered in media and either used or incubated for 24 hours prior to grafting. No specific conditions are recited in the claims to give the claimed characteristics. The same type of cells and matrix are used in Meana and in the specification. Therefore, it is considered that, while not explicitly recited in Meana, the fibroblasts of Meana inherently display the claimed characteristics, including the "wound healing phenotype" recited in the preamble.

Claims 1-15,17-21, 55-60,63-65,67-73,76-78,81-84,85-91,95-99,102-104,107-110 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 02/072113 (IDS).

The instant rejection is not in contradiction to the above lack of enablement rejection. The claims are drawn to a composition and the art is applied to the extent that it appears to read on the claimed composition, particularly claims lacking any required methodology in obtaining the specifically recited

gene expression profile. The specification fails to clearly set forth which methodology results in which expression levels, hence the lack of enablement. However, the art, as set forth below, appears to teach the same methodology, which would inherently result in the claimed characteristics.

'113 teaches human fibroblasts and culturing them on fibrin (7.5 mg.ml)/thrombin-containing matrix for 24 hours. No specific conditions are recited in the claims to give the claimed characteristics. The same type of cells and matrix are used in '113 and in the specification. Therefore, it is considered that, while not explicitly recited in '113, the fibroblast cell composition of '113 inherently display the claimed characteristics, including the "wound healing phenotype" recited in the preamble.

Claims 1-15,17-21, 55-60,63-65,67-73,76-78,81-84,85-91,95-99,102-104,107-110 are rejected under 35 U.S.C. 102(b) as being anticipated by Tuan et al (1996; IDS).

The instant rejection is not in contradiction to the above lack of enablement rejection. The claims are drawn to a composition and the art is applied to the extent that it appears to read on the claimed composition, particularly claims lacking any required methodology in obtaining the specifically recited gene expression profile. The specification fails to clearly set forth which methodology results in which expression levels, hence the lack of enablement. However, the art, as set forth below, appears to teach the same methodology, which would inherently result in the claimed characteristics.

Tuan teaches human foreskin fibroblasts and culturing them on fibrin/thrombin-containing matrix. No specific conditions are recited in the claims to give the claimed characteristics. Human skin fibroblasts were added to a fibrinogen solution. Final concentrations of fibrinogen and fibroblasts were 2.5 mg/ml and 1 x 10^6 cells/ml, respectively. Aliquots (0.1 ml) of the fibroblast/fibrinogen mixtures were placed in wells of 48-well tissue culture plates (Costar, Cambridge, MA) with 1 unit of thrombin per sample. The preparations were subsequently incubated at 37 degrees. The same type of cells and matrix are used in Tuan and in the specification. Therefore, it is considered that, while not explicitly recited in

'113, the fibroblast cell composition of '113 inherently display the claimed characteristics, including the "wound healing phenotype" recited in the preamble.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 79-80 and 105-106 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meana (1998, IDS) in view of Muhart (1999, IDS).

The teachings of Meana are set forth above. Meana did not teach a flexible pounch container. However, Muhart taught packaging a similar wound healing composition in a flexible pouch container for shipping.

One of skill in the art would have found it obvious to combine the teachings of Meana with those of Muhart to arrive at the claimed composition of a matrix of fibroblast cells packaged in a flexible container. One would have been motivated to make such a combination as the container provides a means for storage and transport of the claimed composition.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Valarie Bertoglio/
Primary Examiner, Art Unit 1632